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### EFFECTS OF OXYGEN AND CARBON DIOXIDE ON CARBON MONOXIDE TOXICITY

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## **EFFECTS OF OXYGEN AND CARBON DIOXIDE ON CARBON MONOXIDE TOXICITY**

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**ABSTRACT:** Mean survival time (MST) and fatal blood carboxyhemoglobin (COHb) have been measured in rats exposed to simulated fire atmospheres containing carbon monoxide. Addition of carbon dioxide to the atmosphere decreased MST but did not change the final COHb. Atmospheres with decreased oxygen caused markedly lower MST with an increase in COHb at death. The changes of MST and COHb observed are largely explained by the stimulation of pulmonary ventilation from three sources: 1) decreased inspired oxygen content, 2) the "cellular hypoxia" from increased COHb, and 3) an increased CO<sub>2</sub> of the inspired air.

### **INTRODUCTION**

**F**IRES ABOARD SHIPS lead to the production and accumulation of a complex mixture of toxic components. Acute effects of the toxic environment on crew members in closed spaces of the ship may be rapid, incapacitating and lethal. The composition of the fire atmosphere is partially determined by the chemical composition of the burning material [1], the conditions under which the burning or pyrolysis occurs [2], and the amount of dilution of the fire atmosphere with normal air. Carbon monoxide is the major toxic gas produced by most fires. In confined spaces the decrease in O<sub>2</sub> content and increase in CO<sub>2</sub> associated with combustion contribute in a major way to the physiological response to the fire atmospheres though changes in O<sub>2</sub> and CO<sub>2</sub> do not appear as a serious problem in open fires [3,4].

The present study was done to determine how the toxicity of CO in normal air was changed by increasing the CO<sub>2</sub> content and/or lowering the O<sub>2</sub> of the simulated fire atmosphere. Mean survival time (MST) of rats and fatal blood COHb levels were chosen to measure the relative CO toxicity in the different atmospheres.

### **EXPERIMENTAL**

The 250-300g female rats used were the outbred stock of the Naval Medical Research Institute, NMRI:O(SD)CV. They were maintained on a standard rat chow and water *ad libitum*. Exposures were conducted in groups of 6 rats in a 15-liter glass chamber [5]. The atmosphere in the glass chamber was continuously mixed with a

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small (7 watt) fan. The temperature of the chamber was maintained between 23.5° and 27°C. Control MST [6] values in the absence of CO<sub>2</sub> were determined with mixtures of 0.6% CO in air or in a 14% O<sub>2</sub>-86% N<sub>2</sub> mixture. Experimental MST values were determined with increasing amounts of CO<sub>2</sub> but maintaining a constant O<sub>2</sub> concentration at either 21 or 14% by appropriate reduction in the nitrogen content. Cessation of respiratory movements was taken as the end point and exposure was continued until all 6 rats died. Blood samples for measurement of fatal blood % COHb were obtained from the heart or inferior vena cava with disodium ethylenediamine tetraacetic acid as anticoagulant. Gas chromatograph procedures were used to measure the CO content of the exposure gas [7] and of the blood [8]. Total hemoglobin was determined as cyanmethemoglobin [9].

## RESULTS

The subjective observations of the rats were similar in all exposures. Within two or three minutes after the animals were placed in the contaminated atmosphere there was agitation, and all animals moved about the cage. Most animals lost the ability to walk in about four minutes, and the rats tended to pile on one another rather than just falling on the cage bottom. Only respiratory movements were observed after this time; no muscular convulsions other than gasping were observed during any exposure.

The MST values together with the fatal levels of blood COHb are presented in Table 1. The fatal blood COHb was 85% when the atmosphere contained 21% O<sub>2</sub> and was unchanged in the presence of CO<sub>2</sub>. A significantly higher level of COHb ( $p < 0.01$ ) was observed in 14% O<sub>2</sub>, but this value also was not changed at any CO<sub>2</sub> concentration studied.

*Table 1. Mean Survival Time and Fatal Blood COHb of Rats Breathing 0.6% CO.*

Atmosphere		N <sup>a</sup>	MST <sup>b</sup> Minutes	COHb <sup>c</sup> %
O <sub>2</sub> %	CO <sub>2</sub> %			
21	0	9	22.4 ± 0.8	83.4 ± 0.9
21	2.1	4	18.4 ± 1.1	86.4 ± 0.4
21	4.5	5	16.8 ± 0.6	84.3 ± 0.5
14	0	3	9.6 ± 0.3	89.4 ± 1.0
14	2.3	4	10.1 ± 0.8	90.6 ± 0.4
14	5.4	5	10.4 ± 0.6	90.2 ± 0.4

<sup>a</sup>Number of exposures of 6 rats each.

<sup>b</sup>Mean Survival Time ± Standard Error of the Mean.

<sup>c</sup>Mean % COHb ± Standard Error of the Mean.

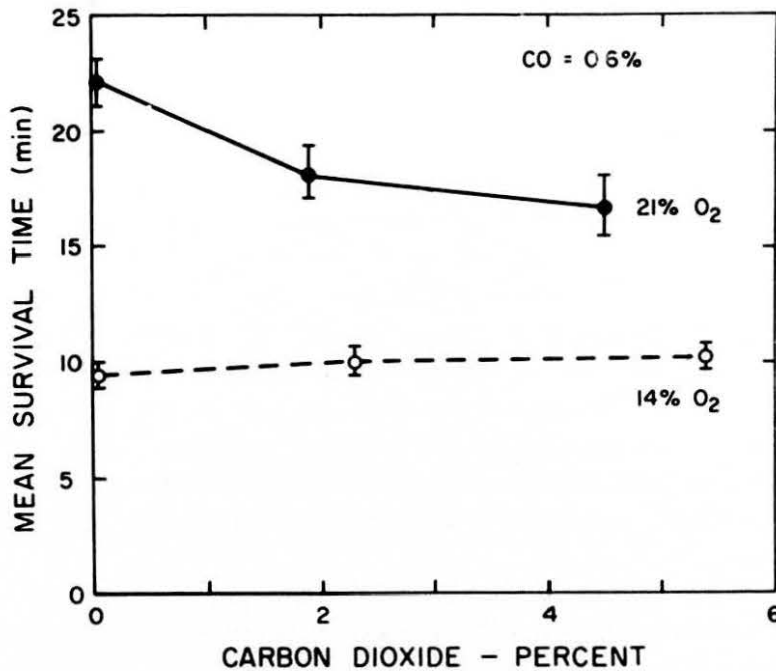


Figure 1. Effects of carbon dioxide on the Mean Survival Time of rats breathing 0.6% carbon monoxide in 21% oxygen (●) and in 14% oxygen (○). The standard error of the mean is indicated by the vertical lines at each concentration of CO<sub>2</sub>.

The data in Figure 1 graphically show the significant decrease in MST caused by decreased O<sub>2</sub> in the absence ( $p \ll 0.01$ ) and in the presence of CO<sub>2</sub> ( $p < 0.01$ ). The addition of 2% CO<sub>2</sub> in the presence of 21% O<sub>2</sub> caused a significant decrease in MST ( $p < 0.02$ ) which was not changed by further addition of CO<sub>2</sub> ( $p > 0.2$ ). Addition of either level of CO<sub>2</sub> in the presence of 14% O<sub>2</sub> did not change ( $p > 0.3$ ) the MST.

## DISCUSSION

A concentration of CO, 0.6%, was chosen to exceed the rat LD<sub>50</sub> for 60-minute exposure [10] and to insure that all animals would die within an hour. The extreme range of individual survival time observed was 6 to 36 minutes. The decreased survival time and increased fatal COHb concentration caused by the 14% O<sub>2</sub> results from two effects. First, due to the extreme hypoxia the hemoglobin in the pulmonary capillary is more highly deoxygenated leading to an increased rate of removal of CO from the alveolar gas. Second, the hypoxic stimulation of pulmonary ventilation brings in a greater volume of contaminated air from which the CO is more effectively absorbed. Low O<sub>2</sub> is expected to increase the rate of COHb change by both effects [11]. These data indicate that hypoxia leads to a marked decrease in MST whether or not there is a simultaneous increase in CO<sub>2</sub>. There was, indeed, no effect of CO<sub>2</sub> over that of hypoxia alone in 14% O<sub>2</sub>.

The experiments in 21% oxygen demonstrate the decrease in MST caused by CO<sub>2</sub> alone. Carbon dioxide is known to stimulate the rate of pulmonary ventilation. Though the extent of such stimulation for rats has not been completely determined, it may reasonably be assumed to be similar to that for man [12]. Carbon dioxide stimulates both the rate and depth of respiration such that there is reproducible increase in pulmonary ventilation with CO<sub>2</sub> concentration. The data of Comroe [12] show that control pulmonary ventilation is increased 1.4 times in 2% CO<sub>2</sub> and 4.9 times in 5% CO<sub>2</sub>. The fall in MST of rats observed here reflects this stimulation of respiration and the extraction of CO from a greater volume of inspired contaminated air. The combined effect in 21% O<sub>2</sub> by 2% CO<sub>2</sub> and the "cellular hypoxia" from the accumulated COHb caused a significant decrease in the measured MST. Physiological limits on this effect are shown by the fact that no further significant decrease in MST was observed by increasing the CO<sub>2</sub> to 5%, though at least a 3-fold increase in pulmonary ventilation [12] would be expected. It was quite clear that respiratory stimulation from "cellular hypoxia" due to the accumulating COHb was important. Even in the absence of CO<sub>2</sub> at 21% O<sub>2</sub> we observed an increased depth of respiration to the degree of "gasping" after 3 to 5 minutes of exposure.

The fatal levels of COHb suggest that the blood was nearly in equilibrium with the inspired air before respiration ceased. An equilibrium maximum COHb of 87.4% and 93.3% breathing 21% or 14% O<sub>2</sub>, respectively, was calculated [13]. Data in Table 1 provide evidence that the COHb reached to within about 3% saturation of the calculated equilibrium values with a high degree of certainty. This is true in all cases even though the MST varied in the extreme from 6 to nearly 40 minutes. These experiments demonstrate that the fatal level of COHb depends upon the inhaled oxygen concentration. Above a certain level of COHb, however, respiration will continue for a shorter time at the more elevated COHb levels.

Fire gas atmospheres, especially in closed spaces, contain lower oxygen with higher carbon dioxide and carbon monoxide than normal air. Data on MST in rats cannot be directly transposed to human reactions. It is clear, however, that hypoxia alone as well as elevated CO<sub>2</sub> cause a decrease in MST. It was also observed that the period of purposeful movements in the rats followed, in a qualitative way, the change in MST. Thus one can expect that the time during which a human could respond to or escape from a fire will be lowered in a similar manner even when fatal levels of COHb are not reached.

#### FOOTNOTES

1. From the Naval Medical Research and Development Command, NNMCM, Department of the Navy, Research Task No. MR041.01.1004-0002. The opinions and assertions contained herein are the private ones of the writers and are not to be construed as official or reflecting the views of the Navy Department or the naval service at large.

2. The experiments recorded herein were conducted according to the principles set forth in the "Guide for the Care and Use of Laboratory Animals", Institute of Laboratory Resources, National Research Council, DHEW Pub. No. (NIH) 74-23.



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